Correlation of Maximum Aortic and Carotid Flow Acceleration in Chronically Instrumented Dogs

By Emmeram Gams, Lee L. Huntsman, and John E. Chimoskey

ABSTRACT

Peak flow acceleration measured in the common carotid artery was compared with peak flow acceleration measured in the ascending aorta of five chronically instrumented dogs. Electromagnetic flow sensors, myocardial electrocardiographic leads, right atrial catheters, and coronary occluders were implanted through an incision of the chest at the fourth intercostal space and a ventral midline incision of the neck under sterile conditions while the dogs were anesthetized with sodium pentobarbital. Experiments began 10 days after surgery. We investigated the response to exercise, to 60-second occlusions of the circumflex branch, the anterior descending branch, or both branches of the left coronary artery, to induction of short-acting barbiturate anesthesia, and to intravenous infusion of three concentrations each of isoproterenol (0.8, 1.5-3.0, and 4.0 µg/min), l-norepinephrine (0.8, 2.0, and 4.0 µg/min), and acetylcholine (0.3-0.5, 0.8-2.0, and 4.0 mg/min). During coronary occlusion, exercise, and induction of anesthesia, both accelerations changed in the same direction and approximately to the same extent. During isoproterenol infusion, both accelerations increased, but the maximum carotid flow acceleration increased more than did the maximum aortic flow acceleration. When l-norepinephrine was infused, the changes were small and were not always in the same direction. When acetylcholine was infused, peak carotid flow acceleration decreased. Peak carotid flow acceleration might be useful as an indirect measure of myocardial mechanical performance during coronary occlusion, anesthesia, and exercise, except during potent peripheral vasodilation like that caused by acetylcholine.

KEY WORDS

carotid artery blood flow coronary artery occlusion l-norepinephrine peak flow acceleration myocardial contractility acetylcholine aortic blood flow barbiturate anesthesia isoproterenol

Maximum acceleration of blood ejected from the left ventricle is a potentially useful measure of left ventricular mechanical performance (1). Maximum flow acceleration in the ascending aorta is as sensitive (2) or more sensitive (3) to a variety of cardiovascular interventions than are stroke volume, peak flow rate, or maximum left ventricular dP/dt. However, peak acceleration of blood ejected from the left ventricle is not yet clinically useful as a measure of ventricular function because of difficulty in measuring blood flow velocity and acceleration in the aortic root in man.

Peripheral arterial flow velocity might provide an indirect method of assessing ventricular ejection dynamics in man. The common carotid artery is suitable for noninvasive measurement of flow acceleration by ultrasonic Doppler flow sensors (4) because of its long, straight, unbranched course through the neck. We have compared changes in maximum flow acceleration measured in the common carotid artery with changes in maximum flow acceleration measured in the aortic root during a variety of cardiovascular interventions that alter both ventricular performance and peripheral resistance. This comparison was initially conducted in acutely prepared, anesthetized dogs (5). The present report deals with the extension of this earlier study to chronically instrumented dogs.

Methods

Five mongrel dogs of both sexes weighing 29-32 kg were anesthetized with sodium pentobarbital (30 mg/kg, iv). Electromagnetic flow sensors were implanted on the
AORTIC AND CAROTID FLOW ACCELERATION

TREADMILL EXERCISE

CORONARY OCCLUSIONS

L-I-NOREPINEPHINE

ISOPROTERENOL

ACETYLCHOLINE

left common carotid artery and the ascending aorta under sterile conditions through an incision of the chest at the fourth intercostal space and a ventral midline incision of the neck. An electrocardiogram (ECG) lead was implanted on the left ventricular surface, and a reference lead was implanted subcutaneously on the chest wall. A polyvinyl catheter was placed in the right atrium. In three dogs inflatable occluders were implanted on the circumflex branch on the left coronary artery and, in two of these three dogs, an occluder was also implanted on the anterior descending branch of the left coronary artery. All catheters and leads were brought out at the back of the chest. The dogs were allowed 10 days to recover from surgery before experiments were begun.

A two-channel square-wave electromagnetic flowmeter (Zepeda Instruments) was employed with an amplitude frequency response of 3 db down at 35 Hz; this frequency response was determined in our laboratory by electronically modulating the carrier wave. Phase angle frequency response was not characterized. Flow accelerations were derived by differentiating the flow signals with electronic differentiating circuits; each of these circuits had a frequency response flat to 50 Hz. This procedure ensured identical processing of both flow signals. The ratio of maximum carotid flow acceleration to maximum aortic flow acceleration was determined electronically with specially designed peak-and-hold and dividing circuits. The ECG was used to trigger a reset circuit so that the ratio was computed on a beat-by-beat basis. The ECG, the flow velocity and acceleration signals, and the ratio of peak carotid flow acceleration to peak aortic flow acceleration were displayed on an oscillograph with a frequency response of 60 Hz.

The following interventions were performed: occlusion of the circumflex branch, the anterior descending branch, or both branches of the left coronary artery for 60 seconds; treadmill exercise at 3.5–4.5 mph for 1–3 minutes; anesthesia induced by administration of the short-acting barbiturate, methohexitol (5.5 mg/kg, iv); and three infusions each of isoproterenol (0.8, 1.5–3.0, and 4.0 μg/min), L-norepinephrine (0.8, 2.0, and 4.0 μg/min), and acetylcholine (0.3–0.5, 0.8–2.0, and 4.0 μg/min).

All flow acceleration data are expressed as percent of the control value which immediately preceded the experimentally induced value. The P values (Fig. 1) are computed using Student's t-test of the mean values of peak carotid and peak aortic flow acceleration.

Results

Figure 1 presents the mean change in peak carotid and peak aortic flow acceleration for each intervention expressed as a percent of the control value. Figure 2 includes six scatter diagrams that summarize the peak flow acceleration data. Figure 3 presents the ratio of peak carotid to peak aortic flow acceleration for each experiment by type of intervention and as a percent of the control ratio; it also illustrates the mean change in the ratio.

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<table>
<thead>
<tr>
<th>Intervention</th>
<th>Flow Acceleration</th>
<th>Ratio</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treadmill</td>
<td>-0.2 to 0.2</td>
<td>1.0</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Coronary Occlusion</td>
<td>-0.05 to 0.05</td>
<td>0.99</td>
<td>0.01</td>
</tr>
<tr>
<td>L-Norepinephrine</td>
<td>-0.1 to 0.1</td>
<td>0.97</td>
<td>0.03</td>
</tr>
<tr>
<td>Isoproterenol</td>
<td>-0.3 to 0.3</td>
<td>0.73</td>
<td>0.001</td>
</tr>
<tr>
<td>Acetylcholine</td>
<td>-0.5 to 0.5</td>
<td>0.42</td>
<td>0.005</td>
</tr>
</tbody>
</table>

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Scatter diagrams of the individual experiments grouped by type of intervention. In each case peak carotid flow acceleration is plotted on the y-axis and peak aortic flow acceleration is plotted on the x-axis. The units on each axis are percent of control.

FIGURE 2
Change of the ratio of peak carotid to peak aortic flow acceleration. Each individual point represents the percent change in the ratio. Each vertical rectangle illustrates the mean percent change (± 1 SD) of the ratio for the number (n) of experiments of each type of intervention. See Figure 1 for abbreviations.

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There are three classes of results according to the direction of change in peak carotid and peak aortic flow accelerations: both increased, both decreased, and one increased while the other decreased. There are two classes of results according to the change in the ratio of peak carotid to peak aortic flow acceleration: very little change and substantial increase.

Exercise and intravenous infusion of isoproterenol cause an increase in both peak carotid and peak aortic flow acceleration. The acceleration response to exercise is illustrated in Figures 1a and 2a. Figure 3a illustrates the very small change in the ratio during exercise. Figure 4 shows an increase in both peak carotid and peak aortic flow acceleration during exercise with essentially no change in the ratio.

The response of peak carotid and peak aortic flow acceleration to isoproterenol infusion is illustrated in Figures 1e and 2e, and the response of the ratio is illustrated in Figure 3e. Both accelerations increased. At the higher infusion rates, the ratio also increased because peak carotid flow acceleration increased more than did peak aortic flow acceleration.

Coronary occlusion and administration of short-acting barbiturate anesthesia are interventions in which both peak carotid and peak aortic flow acceleration decreased but the ratio did not change greatly. The responses of peak carotid and peak aortic flow acceleration to occlusion of the circumflex branch, the anterior descending branch, or both branches of the left coronary artery are shown in Figures 1b and 2b, and the response of the ratio is shown in Figure 3b. Figure 5 shows a decrease in both peak carotid and peak aortic flow acceleration during sequential occlusions of the circumflex branch, the anterior descending branch, and both branches of the left coronary artery. The flow accelerations decreased during all coronary occlusions, and the ratio remained constant during occlusions of the circumflex branch or the anterior descending branch of the left coronary artery. During the second half of the 60-second occlusions of both branches of the left coronary artery, the ratio typically increased because the peak carotid flow acceleration did not decrease as much as the peak aortic flow acceleration decreased.

The administration of short-acting barbiturate anesthesia caused changes in peak carotid and peak aortic flow acceleration (Figs. 1c and 2c); the effect on the ratio of peak carotid to peak aortic flow acceleration is shown in Figure 3c. Although the response of both flow accelerations was triphasic (down, up, down), within a few seconds there was a stable, similar decrease in both peak carotid and peak aortic flow acceleration. Thus, there was little change in the ratio.

Infusion of l-norepinephrine and acetylcholine frequently resulted in a dissociation of the direction of change in peak carotid and peak aortic flow accelerations. L-Norepinephrine-induced changes in peak carotid and peak aortic flow acceleration were small (Figs. 1d and 2d), but frequently peak aortic flow acceleration increased while peak carotid flow acceleration decreased. This change resulted in the small decrease in the ratio of peak carotid to peak aortic flow acceleration (Fig. 3d).

Acetylcholine induced large increases in peak carotid flow acceleration, but peak aortic flow acceleration increased only slightly or decreased (Figs. 1f and 2f). Thus, acetylcholine caused the ratio of the change in peak carotid to peak aortic flow acceleration to increase greatly (Fig. 3f). Figure 6 illustrates the results obtained during acetylcholine infusion: an increase in peak carotid flow acceleration, decrease in peak aortic flow acceleration, and the consequent large increase in the ratio of peak carotid to peak aortic flow acceleration.

Figure 7 summarizes all 178 experiments. Peak carotid flow acceleration is plotted on the ordinate, and peak aortic flow acceleration is plotted on the abscissa; both are expressed as a percent of control. Two correlation coefficients and two regression lines are shown computed with and without the acetylcholine data. The average changes in the ratio of peak flow accelerations were not greater than ± 13% during partial or total left coronary artery occlusion, barbiturate anesthesia, treadmill exercise, l-norepinephrine infusions, or isoproterenol infusion at rates up to 4.0 μg/min. Isoproterenol at the highest infusion rate and all infusion rates of acetylcholine resulted in larger changes in the ratio of peak flow accelerations.

Discussion

These experiments were performed to determine the extent to which peak flow acceleration in the common carotid artery changes in proportion to induced changes in peak flow acceleration in the ascending aorta during various interventions that alter myocardial function and peripheral resistance. Under the conditions of these experiments, both accelerations changed in the same direction and approximately to the same extent except
Response to exercise indicated by the electrocardiogram, arterial blood pressure, carotid flow velocity ($Q_c$), carotid flow acceleration ($dQ_c/dt$), aortic flow ($Q_a$), aortic flow acceleration ($dQ_a/dt$), and the ratio of peak carotid flow acceleration to peak aortic flow acceleration. High-speed record of individual complexes on the left is followed by a low-speed record of the envelope of the several wave forms. There are two periods of exercise bracketed by periods of sitting and standing at rest. There is no change in the ratio of peak carotid to peak aortic flow acceleration during any portion of the record.

Response to coronary occlusion. The variables shown are the same as those shown in Figure 4, except that the arterial blood pressure trace has been omitted. The response to a 60-second occlusion of the anterior descending (L. A. D.) and the circumflex (L. C.) branches of the left coronary artery are shown separately and together. The ratio of peak carotid to peak aortic flow acceleration does not change during occlusion of the anterior descending or the circumflex branches of the coronary artery but increases during the second half of occlusion of both of these branches, because peak carotid flow acceleration decreases less than peak aortic flow acceleration decreases.
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FIGURE 6

Response to infusion of acetylcholine. The variables shown are the same as those shown in Figure 4. The responses to two infusion rates of acetylcholine (0.8 mg/min and 2.0 mg/min) are shown. Peak carotid flow acceleration increases and peak aortic flow acceleration decreases, resulting in a large increase in the ratio of peak carotid flow acceleration to peak aortic flow acceleration.

When peripheral resistance increased with \( l \)-norepinephrine infusion or decreased with acetylcholine infusion. During infusion of these two agents the direction of change in peak flow acceleration at the two sites frequently dissociated. During infusion of \( l \)-norepinephrine the magnitude of the changes was small. However, during infusion of acetylcholine there was a large increase in peak carotid flow acceleration with only a small increase or a decrease in peak aortic flow acceleration. The higher infusion rates of isoproterenol caused a much larger increase in peak carotid flow acceleration than it did in peak aortic flow acceleration, probably by reduction of peripheral resistance.

Although this study did not attempt to evaluate the validity of the concept that peak aortic flow acceleration is the most sensitive index of ventricular performance, it is important that peak aortic flow acceleration be established as an index of myocardial mechanical performance. Rushmer (1) has demonstrated that peak aortic flow acceleration is decreased in unanesthetized dogs when a coronary artery occlusion.

FIGURE 7

Scatter diagram of 178 experiments. Ordinate and abscissa are similar to those in Figure 2. The acetylcholine data are encircled. The correlation coefficient \( r = 0.78 \) and the regression line \( y = 1.05x + 13.35 \) for all 178 experiments improved to \( r = 0.89 \) and \( y = 1.1x + 1.3 \) when the acetylcholine data were excluded and only 152 experiments were considered.
artery is occluded, and Noble and co-workers (3) have shown that peak aortic flow acceleration is more sensitive than is peak flow rate, stroke volume, or left ventricular peak dP/dt during coronary occlusion or intracoronary infusion of calcium gluconate or isoproterenol. In experiments by Nutter and colleagues (2) maximal acceleration of aortic blood flow has been demonstrated to be a sensitive index of ventricular performance during induced alterations in the inotropic state and in preload. Peak aortic flow velocity, peak aortic flow acceleration, and stroke volume data from chronic animal experiments in our laboratory essentially agree with this concept.

Peak aortic flow acceleration is an index of myocardial mechanical performance because, during the accelerating phase of cardiac ejection, the force opposing ventricular contraction is the inertia of the blood mass. This conclusion is drawn from the observation (6, 7) that ventricular pressure exceeds aortic pressure only during the brief interval between the opening of the aortic valve and the time when peak ascending aortic flow is attained; during this interval the blood is being accelerated.

The extent to which changes in peak aortic flow acceleration result in proportional changes in peak carotid flow acceleration depends not only on ventricular function but also on the characteristics of the peripheral blood vessels. Unfortunately, the relative contribution of changes in large vessel compliance and changes in peripheral resistance to changes in carotid flow acceleration is not known. However, we observed a large change in the ratio of peak carotid to peak aortic flow acceleration and a dissociation of the direction of change in the two peak flow accelerations when potent vasoactive agents were administered. This phenomenon was seen in these chronic dog studies during infusions of acetylcholine and norepinephrine and during the largest infusion of isoproterenol; it was also observed in acute experiments when papaverine, acetylcholine, histamine, and trimethaphan camphorsulfonate were administered (5). Nevertheless, in both acute (5) and chronic preparations, a variety of interventions that alter myocardial mechanical performance result in proportional changes in peak carotid and peak aortic flow accelerations. Similar results for maximal flow accelerations in the femoral artery and the aortic root have been reported by Baan and co-workers (8) for a limited number of interventions in the acute dog preparation.

Although agents which have profound resistance effects render carotid flow acceleration an unreliable index of aortic flow acceleration and, thus, of myocardial mechanical performance, there are clinical situations, i.e., anesthesia, exercise, and coronary occlusion, in which the peripheral flow acceleration is a reliable index of myocardial performance.

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**References**

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